(FILE 'HOME' ENTERED AT 09:02:02 ON 21 NOV 2001)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 09:02:15 ON 21 NOV 2001

L1	5339095	S PROTEIN?
L2	104174	S L1 AND MATURE
L3	153	S L2 AND VEGF
L4	0	S L3 AND PROTEASES
L5	3	S L3 AND PROTEASE?
L6	3	S L3 AND (HEPARIN OR CHO CELLS)
L7	10	S L3 AND CLEAV?
L8	3	DUP REM L7 (7 DUPLICATES REMOVED)
L9	49529	S L2 AND (PROCESS? OR CLEAV? OR PRODUC?)
L10	22528	S L9 AND (DIFFER? OR DISTINCT? OR FORMS)
L11	6337	S L9 AND (PROTEO?)
L12	2821	S L10 AND (PROTEO?)
L13	40668	S L2 AND (DIFFER? OR DISTINCIT? OR MORE THAN ONE)
L14	8899	S L2 AND (FORMS)
L15	212	S L2 AND (DIFFERENT FORMS)
L16	3	S L15 AND REVIEW
L17	131	S L9 AND (DIFFERENT FORMS)
L18	0	S L17 AND (VEGF OR VASCULAR ENDOTHELIAL GROWTH FACTOR)
L19	75	S L13 AND (VEGF OR VASCULAR ENDOTHELIAL GROWTH FACTOR)
L20	38	DUP REM L19 (37 DUPLICATES REMOVED)
L21	6531	S L2 AND (PROTEASE?)
L22	13	S L21 AND DIFFERENT FORMS
L23	7	DUP REM L22 (6 DUPLICATES REMOVED)

Vascular endothelial growth factor-D (**VEGF**-D), the most recently discovered mammalian member of the **VEGF** family, is an angiogenic **protein** that activates **VEGF** receptor-2 (VEGFR-2/Flk1/KDR) and VEGFR-3 (Flt4). These receptor tyrosine kinases, localized on vascular and lymphatic endothelial cells, signal for angiogenesis and lymphangiogenesis. **VEGF**-D consists of a central receptor-binding **VEGF** homology domain (VHD) and N-terminal and C-terminal propeptides that are **cleaved** from the VHD to generate a **mature**, bioactive form consisting of dimers of the VHD. Here we report characterization of mAbs raised to the VHD of human **VEGF**-D in order to generate **VEGF**-D antagonists. The mAbs bind the fully processed VHD with high affinity and also bind unprocessed **VEGF**-D. We demonstrate, using bioassays for the binding and cross-linking of VEGFR-2 and VEGFR-3 and biosensor analysis with immobilized receptors, that one of the mAbs, designated VD1, is able to compete potently with **mature VEGF**-D for binding to both VEGFR-2 and VEGFR-3 for binding to **mature VEGF**-D. This indicates that the binding epitopes on **VEGF**-D for these two receptors may be in close proximity. Furthermore, VD1 blocks the mitogenic response of human microvascular endothelial cells to **VEGF**-D. The anti-(**VEGF**-D) mAbs raised to the bioactive region of this growth factor will be powerful tools for analysis of the biological functions of **VEGF**-D.

28 ANSWER 15 OF 20 MEDLINE
AN 89137779 MEDLINE
DN 89137779 PubMed ID: 3066674
TI Human interleukin-3 and granulocyte-macrophage colony stimulating factor: site-specific mutagenesis and expression in yeast.
AU Cosman D; Deeley M C; Price V; Klinke R; Clevenger W; Hemenway T; Anderson D; Sassenfeld H; Urdal D L
CS Immunex Corporation, Seattle, Washington 98101.
SO DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1988) 69 9-13. Journal code: E7V; 0427140. ISSN: 0301-5149.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198903
ED Entered STN: 19900306
Last Updated on STN: 19900306
Entered Medline: 19890327
AB The two human colony stimulating factors, interleukin-3 and granulocyte-macrophage colony stimulating factor, have been molecularly cloned and expressed as secreted proteins in yeast. In both cases, non-glycosylated and glycosylated forms of the molecules were produced. Removal of N-linked glycosylation sites from the genes by site-directed mutagenesis prevented addition of most of the sugar residues, but revealed a low level of residual O-linked glycosylation on a portion of the molecules. No difference in specific biological activity was found between the **different forms** of the proteins. It was found that a significant proportion of human granulocyte-macrophage colony stimulating factor was degraded by the yeast KEX2 protease that was cleaving after the dibasic sequence Arg-Arg at positions 23-24 of the **mature protein**. Site-specific mutagenesis was employed to change this sequence to Leu-Arg, and this change resulted in greatly increased expression levels of full length protein and biological activi

mature form depends on the host cell. Your arguments relate to the protien without the signal sequence, however, this is different than "matur" which is the finally processed protein. Although the expression of the plasmid encoding the full length prtoien would produce the mature protein, said mature protein would depend on the host cell, and applicant have not provided a written description of how that mature protein would look like. Cho cells process vegf differently and produces a mature form of the protein without the heprin binding domian, which would not have been predicted. Using bacterial host cells like e-coli process proteins differently than other host cells like mammalimna or insects.

Search: proteases and mature, vegf, heparin and cho cells